Guillain-Barre syndrome associated with COVID-19 and malaria coinfection: A case report

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Abstract

We reported the first case of Guillain-Barré syndrome that is associated with COVID-19 and malaria coinfection. The current report demonstrates diagnostic challenge to identify GBS case in a country like Sudan that is endemic with several infectious diseases associated with developing GBS.

Brief Report

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Consent for Publication

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Abstract:

We reported the first case of Guillain-Barré syndrome that is associated with COVID-19 and malaria coinfection. The current report demonstrates diagnostic challenge to identify GBS case in a country like Sudan that is endemic with several infectious diseases associated with developing GBS.

Keywords: Neurology; emerging infectious disease; COVID-19 and Malaria coinfection; Guillain-Barre syndrome; Neurological manifestation; Integrated Program for Disease Control; Sudan

Introduction:

Guillain-Barre syndrome (GBS) is considered the most common cause of acute flaccid paralysis worldwide.[1] Most patients are presented with an antecedent illness, mostly upper respiratory tract infections, which occur in accordance with the onset of motor weakness.[2] Numerous endemic and emerging pathogens have been associated with developing GBS worldwide. Several microbes including parasites, bacterial, and viral infection are associated with developing GPS including diseases of high prevalence such as malaria, *Campylobacter jejuni* infection, Zika virus, and recently COVID-19.[3–6] Additionally, the development of GBS is associated with several arboviral diseases including Chikungunya, Crimean–Congo hemorrhagic fever (CCHF), dengue, Rift Valley fever, and West Nile virus.[6–10] Other viral infection such as hepatitis E virus, Epstein-Barr virus (EBV), cytomegalovirus (CMV) were involved in the development of GBS.[11] Furthermore, other infectious diseases such as Helicobacter pylori, leishmaniasis, and onchocerciasis are also associated with GBS manifestation.[12–14]

Unfortunately, a wide range of infectious diseases that are associated with GBS are endemic in Sudan, particularly arboviral and emerging viral diseases.[15,16] In addition to the recently emerging COVID-19 infection, endemic viruses associated with GBS that are endemic in the country include Chikungunya, CCHF, dengue, and Rift Valley fever as well as EBV, hepatitis E, West Nile, and Zika viruses.[17–26] Other Sudan-endemic infectious diseases that are associated with GBS include Helicobacter pylori, leishmaniasis, malaria, and onchocerciasis.[17,27–31] However, cases of GBS recently reported in Sudan were associated with COVID-19 infection.[32]

In this communication, we report a case of a 41-year-old female diagnosed with GBS associated with COVID-19 and malaria co-infection in Sudan.

Case presentation:

A 41-year-old female with a pre-existed medical history of type 2 diabetes has arrived at the emergency unit of Royal Care Hospital in Khartoum state, Sudan presented with fever, chills, headache, productive cough, diarrhoea, lower limb weakness, and back pain.

The weakness progressed to the upper limbs within 24 hours. She reported that, in the previous seven days, she experienced fatigue, headache, fever and chills, and she received paracetamol. She had a normal pulse rate (76/min), respiratory rate (17/min), blood pressure (90/50), and temperature (39°C). Neurological examinations showed generalized areflexia and down-going plantar reflexes. The muscle power assessment scale (MRCS) was 0/5 in the upper limbs and the lower limbs. A computed tomography scan of the thorax revealed bi-basilar consolidation and patchy peripheral ground-glass opacities in line with classic COVID-19 infection. Her nasopharyngeal swab was positive for SARS Cov-2 with real-time polymerase chain reaction assay (RT-PCR). Other viral infections associated with developing GBS were excluded using multiple RT-PCR assays. Similarly for the associated parasitic infections, they were excluded except for malaria which

was positive. Her full blood count revealed leucopenia, high C-reactive protein (40mg/L), blood film showed asexual stage trophozoites of *Plasmodium falciparum* and ICT was also positive (Figure 1). The CSF showed E-protein without cells. The electromyography (EMG), on the 2nd day after admission, showed a demyelinating pattern.

For the treatment, the patient received intravenous immunoglobulin (IVIG) (0.4 g/kg/day for five days), and a paracetamol infusion for the back pain. For the malaria infection, the patient received artemether/lumefantrine four tablets (20 mg artemether; 120 mg lumefantrine per tablet) orally (PO) as an initial dose, followed by four tablets PO 8 hours after the initial dose, then four tablets PO twice daily (morning and evening) for two days for a total course of 24 tablets. She responded well after three days. Upper and lower limbs showed an improved power grade (3/5).

Discussion:

Guillain-Barre syndrome (GBS) is an immunologically mediated, acute inflammatory demyelinating polyneuropathy.[33] It is the most common cause of acute flaccid paralysis, associated with an antecedent infection, especially viral infections.[4,32]Other causative agents include bacterial infections such as Mycoplasma;*Campylobacter jejuni* , *Haemophilus influenza* , and*Rickettsia rickettsi* are well-recognized bacterial agents.[3] Furthermore, GBS has been reported to be associated with parasitic infections including *Leishmania donovani* , *Plasmodium falciparum,* and *P. vivax.* [5]

In Sudan, the diagnosis of GBS is challenging due to the limited resources and diagnostic capacity in the country, therefore, most of physicians relies heavily on the clinical diagnosis.[32]Unfortunately, this implies that many other cases of GBS might have been missed due to the lack of experienced physicians during patients' presentations, particularly in the remote areas of the country.

This study reported a case of typical GBS preceded by classic signs and symptoms of biologically confirmed COVID-19 and malaria caused by*Plasmodium falciparum* . In this case, the development of GBS could be attributed to the confirmed infections, as both were reported to contribute in GBS manifestation.[1,5,32]

The first symptoms of GBS in this case, were lower limb weakness, back pain and paraesthesia. Generalized flaccid paraparesis, or tetraplegia, evolved over a period of one to two days in our patient. Furthermore, she had leucopenia, which is associated with malaria and COVID-19 infections.[34,35]

Malaria can be associated with atypical neurological manifestations which may include cerebellar ataxia and post-malaria neurological syndrome, and a few studies have reported the association of *P. falciparum* and *P. vivax* with GBS.[36–38]Unfortunately, most of Sudan is hyperendemic with malaria.[17,29,31] This combined with the recent emergence and spread of COVID-19 is alarming and requires that healthcare providers in theses hyperendemic areas to pay extra attention to the neurological syndromes and the possible involvement of GBS.

Immune-mediated damage is considered the mechanism of developing GBS.[39] In malaria infection, the asexual stage of the parasite is accompanied by release of cytokines and other mediators, which in turn trigger an inflammation that affects the axons leading to demyelination. This might explain the involvement of malaria infection in developing GBS, alternative explanation is that the occurrence of GBS is attributed to the occlusion of vasa-nervosum by the malaria parasites or by the formed immune complex.[36–38]

More studies are needed to further understand the mechanisms of developing GBS due to malaria and/or COVID-19 infections, and the severity and clinical course of GBS. This will impact case management strategies, especially in cases where GBS is more severe.

Countries endemic with several infectious diseases that are associated with GBS are facing huge diagnostic challenge, particularly countries with limited resources like Sudan. The wide spectrum of GBS-associated infections endemic in Sudan is beyond the country current capacity to prevent and control. This is further indicated by the persistently increased rate of infectious diseases outbreaks in the country.[17–20,22,29,31,40–42] Therefore, it would be more realistic and achievable to invest more resources on improving the diagnostic

capacity, surveillance systems, case management, and early reporting to engage partners and collaborating institutes in the response.[43] This could be achieved the integration of diseases control programs.[44] Particularly people lives in humanitarian crisis settings with severe gaps in essential services are crucial need for such integration.

Building healthcare professionals' capacity to recognise the early signs and symptoms of GBS, as well as the potential relationship between GBS and preceding infections such as malaria and COVID-19 will enable earlier diagnosis, prompt treatment and case managment might lead to better disease outcomes. There is also a need for a national GBS differential diagnosis protocol and treatment guideline to ensure that patients are timely identified and receive a high quality care.

Conclusion

Here, we report a case of GBS associated with malaria and COVID-19 co-infection. Considering that, both diseases are associated with GBS, on this case; it was challenging to attribute the GBS either one of the infections. Furthermore, GBS is considered a rare condition, this could be far from true but due to under-diagnosis and under-reporting. This urges for further studies to investigate the burden and risk factors associated with GBS in Sudan.

The current report demonstrates the first case of GBS that is associated with COVID-19 and malaria co-infection in Sudan. Therefore, healthcare providers need to be vigilant toward the neurological manifestation of all infectious diseases that associated with neurological syndromes including GBS for the early detection and a better case management.

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